N.D.

PRELIMINARY SURVEY OF CANCER RATES IN A COMMUNITY EXPOSED TO LOW LEVELS OF CREOSOTE COMPONENTS IN MUNICIPAL WATER

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The Minneapolis-St. Paul area, including St. Louis Park, was part of the Third National Cancer Survey (14) conducted for the three years, 1969 to 1971. All hospital records in the five county Twin Cities area were searched for cancer diagnoses, and abstracts of cancer records were coded on computer tape. Because of the availability of these records on tape, albeit for a limited three year period of time, it was decided to compare cancer incidence rates in St. Louis Park with those in the nearby municipalities of Edina and Richfield and in the entire Minneapolis-St. Paul Standard Metropolitan Statistical Area (SMSA).

METHODS

Incidence rates for 45 types or sites of cancer were calculated for St. Louis Park, Edina, Richfield, and the Minneapolis-St. Paul SMSA using data from the Third National Cancer Survey for the three years, 1969-1971. Richfield was selected because it was a SMSA suburb similar to St. Louis Park in social and economic characteristics such as median school years completed, percent high school graduates, occupation and median and mean family income. Edina was selected because the creosote contamination was believed, at that time, to be moving toward Edina. The entire SMSA was used as the major comparison area. Incidence rates were age-adjusted to the SMSA populations of white males and white females respectively. Calculations were done of average annual age- and sex-specific cancer incidence rates, age-adjusted incidence rates, standard incidence ratios (SIR), Mantel-Haenszel overall summary Chi-squares (15, 16) and Z statistics. The latter two statistics are used to assess the significance of the difference between two rates after adjusting for age. Population denominator data were taken from the 1970 U.S. Census (17).

RESULTS

For males, no cancer rates in St. Louis Park were statistically significantly different fromthose in the three comparison areas. Among females, age-adjusted

In November, 1978, the Minnesota Department of Health detected minute (nanogram per liter) quantities of various polynuclear aromatic hydrocarbons (PAH), including pyrene, fluoranthene, anthracene, and naphthacene, in several municipal and industrial wells in the city of St. Louis Park, a suburb of Minneapolis (1). Although there are no official U.S. standards for PAH in water supplies, four municipal wells were closed immediately because the amounts exceeded the World Health Organization's recommendation for safe levels in drinking water (2). PAH compounds were not detected in the remaining ten municipal wells.

The PAH compounds apparently originated from the site of a plant which distilled coal-tar products and treated wood with creosote from 1917 to 1972. During this time, wastes from the plant's operations were deposited on the surface of the site, allowing contamination of the groundwater reservoirs below.

It is not known how long PAH compounds have been in the St. Louis Park water supply, since techniques for their detection in water have only been available in the past few years (3). A well drilled in 1932, however, was shut down within a few months due to a creosote-like odor and taste of the water, and it is possible that PAH compounds have been in the municipal water for many years or decades in low concentrations.

The occurrence of PAH in the environment is of concern because of their demonstrated carcinogenicity for animals and/or mutagenicity for bacteria (4-9). There appear to be no epidemiologic studies of human populations exposed to low levels of PAH in water supplies, although the association of occupational skin cancer with creosote and coal-tar compounds has long been known (10-13).

rates for all cancer sites combined, for breast cancer, and for cancers of the gastrointestinal tract were higher in St. Louis Park than in Edina, Richfield, and the SMSA. The excess in gastrointestinal cancer rates for females was only slightly significant ($P < .05$) but both all cancer sites combined and breast cancer had differences with a high degree of statistical significance ($P < .005$). Further details of the significant comparisons are given in Table I.

DISCUSSION

In the absence of epidemiologic literature on ingested exposure to PAH, it is of interest to note that rats fed one PAH compount--e-methylcholanthrene--develop mammary carcinoma in high frequency and these tumors occur almost exclusively in females (18-20). Other PAH compounds produce a variety of tumors in animals (4).

Breast cancer rates vary considerably with geographic location and with characteristics of the population (21-24). In the Third National Cancer Survey (14), for example, the rates varied from 59 to 83 per 100,000 white females per year in the nine different study areas. In a recent review of the epidemiology of human breast cancer, Kelsey has summarized the influence of major factors known to influence breast cancer rates, expressing the results as relative risks (RR)--the ratio of case rates in a population with the factor to the rate in those without the factor (24). These include: 1. First degree relative with breast cancer (RR of 2-4); 2. Absence of or late age at first full-term pregnancy (RR of 2-4); 3. History of fibrocystic disease of the breast (RR of 2-4); 4. Exposure to high levels of radiation to the chest (RR of 2-4); 5. Upper socio-economic class (RR of 2-4); 6. Obesity (RR of 2-4); and 8. Early age at menarche and late age at menopause (RR of 1.1 - 1.9). Rates given in the literature for Jewish populations are contradictory, varying

from less than to higher than those for non-Jewish whites (25-27). The contribution of these factors to the difference in breast cancer rates between St. Louis Park and the comparison areas cannot be evaluated without further information about the individual cases. Because of the sizeable population with Jewish ancestry, estimated to be 20% in 1971 (28), the influence of this factor is of particular interest, but would not explain the 1.5 fold difference in rates even if 20% of the St. Louis Park breast cancer cases were Jewish and a two-fold relative risk existed.

The lack of elevation in the rates for the great majority of cancer types is reassuring, but factors responsible for the elevation in breast cancer rates in St. Louis Park need to be investigated. Further interpretation must await interviews of the 95 cases of breast cancer or their families and an appropriate control group. The results of such a detailed case-control study, now in the planning phases, may explain the elevated breast cancer rates in St. Louis Park on the basis of the frequencies of known risk factors. If this is not the case, further studies to explore a possible relationship with the water supply must be considered.

At the present time, the elevated incidence of breast cancer cannot be attributed to the water contamination, although the limited information available does not rule out such an association. It should be noted that the wells found to be contaminated have been closed, presumably reducing any hazard which may have been present.

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TABLE I

Cancer Incidence Rates for Total Cancers and Breast Cancer
St. Louis Park and
Three Comparison Populations
White Females Only, 1969 to 1971

		Breast Cancer		All Cancers	
	Population	Total Cases 1969-1971	Average Annual Age-Adjusted Rate* per 100,000 pop.	Total Cases	Average Annual Age-Adjusted Rate* per 100,000 pop.
St. Louis Park	25,424	95	123	301	381
Edina	22,492	65	82	175	241
Richfield	24,247	41	58	145	235
MSP SMSA	914,218	2130	78	7726	282

*Rates per 100,000 white females, adjusted to the MSP SMSA population of white females, 1970.

Mantel-Haenszel Summary Chi-Square Values and ρ-Values

	CHI-SQUARE		ρ-VALUE	
Comparison	Breast Cancer	All Cancers Females	Breast Cancer	All Cancers Females
St. Louis Park vs Edina	3.38	19.90	.05 < ρ < .1	< .0005
St. Louis Park vs Richfield	10.85	21.18	.001	< .0005
St. Louis Park vs SMSA	13.64	24.31	< .0005	< .0005

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Computer Format

1. Arrange sites by organ system using the site or site and histology codes given.

2. TABLES WITH 3 YEAR TOTAL NUMBER OF CASES 1969-1971

   By sex for each city, make a separate table with the total number of cases per age interval and for all ages for each individual site of cancer, for each organ system and for all sites combined.

3. TABLES WITH AVERAGE ANNUAL INCIDENCE RATES/100,000 1969-1971

   By sex for each city, make a separate table of <u>average</u> annual age and sex-specific incidence rates per 100,000 population for each individual site of cancer, for each organ system and for all sites combined.

4. TABLES WITH AVERAGE ANNUAL AGE - ADJUSTED INCIDENCE RATES/100,000 1969-1971

   By sex for each city, make a separate table of average annual age-adjusted rates per 100,000 population for each individual site of cancer, for each organ system and for all sites combined. Use the direct method of adjustment: apply the <u>average</u> annual age and sex-specific incidence rates per 100,000 of study population to the respective proportions of the population in that age and sex group in the standard population (Mpls. - St. Paul SMSA).

   Eg. $\sum_{i=1}^{9} \frac{riPi}{P} = \sum_{i=1}^{9} \left(\frac{Pi}{P}\right)_{ri}$

5. STANDARDIZED MORBIDITY RATIO CACULATION

   By sex for each city, multiply the number of persons within each age group of the study population by their respective average annual age and sex specific incidence rates per 100,000 of the standard population (Mpls. - St. Paul SMSA), then sum and divide by 100,000 to obtain the expected number of cases per year.

   SMR (standardized morbidity ratio) = $\frac{\text{observed \# of cases per year}}{\text{expected \# of cases per year}}$

   Do this for individual sites of cancer, organ systems and all sites combined.

6. Z STATISTIC CALCULATION

Change all 3 year case numbers that are zero to .5 (½ of a person). Then by sex for each comparison (SLP-E, SLP-R, E-R), calculate a Z statistic using 3 year age-adjusted rates. We will use a standard normal table to interpret these results.

$$Z = \frac{\left| \text{adjusted rate 1} - \text{adjusted rate 2} \right|}{\sqrt{\text{variance (adj. rate 1)} + \text{variance (adj. rate 2)}}}$$

where the variance (adj. rate) $= \sum_{i=1}^{9} \left(\frac{Pi}{P}\right)^2 \left(\frac{ri\ (1-ri)}{ni}\right)$

where r = age and sex specific rate and n = denominator of r.

7. MANTEL - HAENZEL SUMMARY CHI - SQUARE CALCULATION

Use the Mantel-Haenzel method to calculate overall summary chi-squares for the six comparisons given (SLP-E, SLP-R, SLP- SMSA, E-R, E- SMSA, R-SMSA). This method should be executed on the total number of cases for the 3 year period. Indicate with an asterisk any values significant at the 5% level. See separate paper for method.

8. Print the following information on SLP cases, arranged by census tract:

   a. address

   b. age at dx

   c. sex

   d. case #

   e. date of 1st dx

   f. primary site and histologic type

   g. method of dx

Calculate an overall summary chi-square for the following comparisons:

1. St. Louis Park vs. Edina
2. St. Louis Park vs. Richfield
3. St. Louis Park vs. SMSA
4. Edina vs. Richfield
5. Edina vs. SMSA
6. Richfield vs. SMSA

Mantel-Haenzel Method *

1. Given i = age interval, i = 1,9; j = sex, j = 1,2; k = city, k = 1,4

i = 1 = < 15	j = 1 = male	k = 1 = St. Louis Park
2 = 15-24	2 = female	2 = Edina
3 = 25-34		3 = Richfield
4 = 35-44		4 = Mpls-St. Paul SMSA
5 = 45-54		
6 = 55-64		
7 = 65-74		
8 = 75-84		
9 = 85+		

2. By sex for each city determine the total # cases, 1969-1971, per age interval, n_{ijk}.
3. By sex for each city determine the population per age interval, p_{ijk}.
4. By sex for the two comparison cities determine their combined # cases per age interval, $N_{ij} = n_{ijk} + n_{ijk'}$.
5. By sex for the two comparison cities determine their combined population total per age interval, $P_{ij} = p_{ijk} + p_{ijk'}$.
6. By sex for the two comparison cities determine their mean incidence rate for each age interval, $R_{ij} = \frac{N_{ij}}{P_{ij}}$.
7. By sex determine the expected # cases per age interval for <u>one</u> of the two comparison cities, $E_{ijk} = R_{ij}p_{ijk}$.
8. By sex determine the observed # cases per age interval for the same city, $O_{ijk} = n_{ijk}$.

9. By sex determine the variance of the observed # cases minus the expected # cases for each age interval,

$$V(O_{ijk}-E_{ijk}) = \frac{(p_{ijk})\ (p_{ijk}')\ (N_{ij})\ (P_{ij}-N_{ij})}{(P_{ij})2\ \ (P_{ij}-1)}$$

10. By sex for the two comparison cities calculate an overall summary chi-square,

$$X^2(1) - \frac{[\ |\sum_i O_{ijk} - \sum_i E_{ijk}| - .5]^2}{\sum_i V(O_{ijk}-E_{ijk})}$$

11. Evaluate the chi-square value thus obtained and if the value is >3.84, use an asterisk to indicate that it is significant at the 5% level.

12. Calculate an overall summary chi-square for the comparison of two age- and sex-adjusted rates,

$$X^2(1) = \frac{[\ |(\sum_i O_m + \sum_i O_f) - (\sum_i E_m + \sum_i E_f)| - .5]^2}{\sum_i V(O-E)_m + \sum_i V(O-E)_f}$$

13. Evaluate the chi-square value thus obtained and if the value is >3.84, use an asterisk to indicate that it is significant at the 5% level.

14. Repeat this procedure for each of the six comparisons specified.

* Apply this method to individual sites of cancer, organ systems, and to all sites combined.

Sites arranged by organ system. Site and histology codes from the Manual of Tumor Nomenclature and Coding, 1968 edition.

	Site Code	Computer Code
I. Buccal Cavity and Pharynx	400-490	4
lip	400-409	40
tongue	410-419	41
salivary gland	420-429	42
gum and mouth	430-459	43-45
nasopharynx, other pharynx and tonsil	471-479,461-469, and 480-489	46-49
II. Digestive System	500-584 not 588-589	5
esophagus	500-509	50
stomach	510-519	51
small intestine	520-529	52
colon, exc. rectum	531-539,544	53
rectum and rectosigmoid jct.	540-541	54
liver	550	55
gallbladder	560	11
other biliary	551,561-569	56
pancreas	570-579	57
III. Respiratory System	600-624	6
larynx	610-619	61
lung, bronchus, trachea	620-624	62
IV. Bones and Joints	700-709	70
V. Soft Tissues	710-719	71
VI. Melanomas of Skin	730-739 (types 8721-8783)	73
VII. Breast	740-749	74
VIII. Female Genital System		8001
cervix invasive	800-809	80
corpus uteri	820	12
uterus, NOS	829	82
ovary	830	83
vagina	840	13
vulva	842-843	84

		Site Code	Computer Code
IX.	Male Genital System		8002
	prostate	859	85
	testis	869	86
	penis	870	87
X.	Urinary System	889-898 not 899	8003
	bladder	889	88
	kidney and renal pelvis	890-891	89
XI.	Eye and Orbit	900-909	90
XII.	Brain and Other Nervous System		9001
	brain	910-919 not 9531-9533	91
	other nervous system	920-929	92
XIII.	Endocrine System	930-940	9002
	thyroid	930-931	93
	other endocrine system	---	---

The MOTNAC site codes for the following are 960-969, nodes.

	Histology Code	Computer Code
XIV. Lympho & Reticulum Cell Sarcoma	9611-9643	14
lymphosarcoma, NOS	9613	141
lymphocytic lymphosarcoma	9623	142
lymphoblastic lymphosarcoma	9633	143
reticulum cell sarcoma, NOS	9643	144
XV. Hodgkin's Disease	9653-9683	15
hodgkin's disease, NOS	9653	151
hodgkin's disease, lum.-his.predominance	9654	152
hodgkin's disease, mixed cellularity	9655	153
hodgkin's disease, lym. depletion	9657	154
hodgkin's disease, nodular sclerosis	9658	155
hodgkin's paragranuloma	9663	156
hodgkin's granuloma	9673	157
hodgkin's sarcoma	9683	158
XVI. Other Lymphomas	9591-9603,9691-9693, 9711-9723,9741-9763	16
lymphoma, NOS	9593	161
sten cell lymphoma (no cases)	9603	162
giant follicle lymphoma	9693	163
Burkitt's tumor (no cases)	9753	164
lymphosarcoma ending in leukemia	9763	165

The MOTNAC site code for the following is 698, RES.

reticuloendothelial sarcoma	9723	166
microglioma (no cases)	9713	167
mast cell sarcoma	9741-9743	168

The MOTNAC site codes for the following are 730-739, skin.

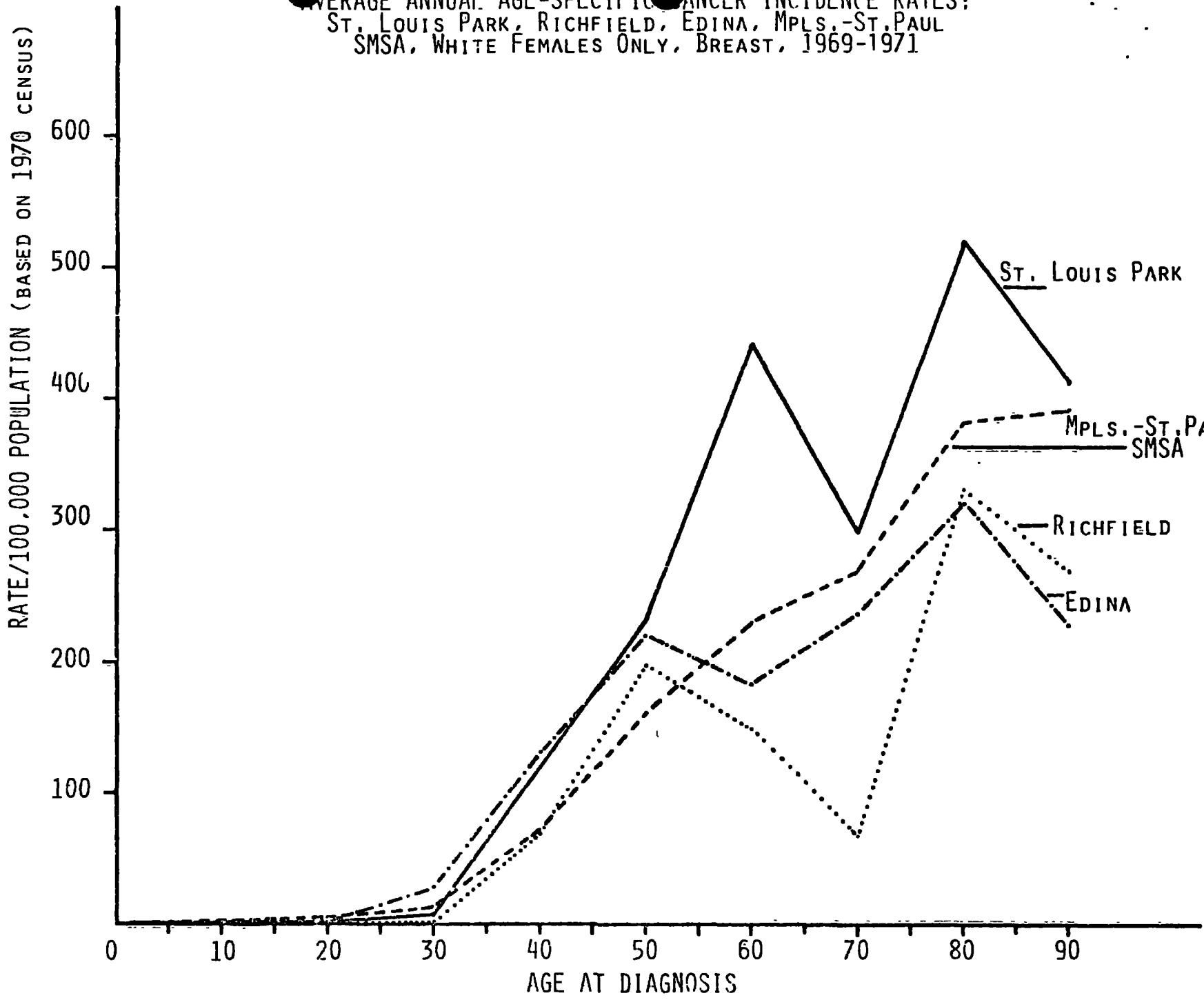
XVII. Mycosis Fungoides	9703	17(171)

The MOTNAC site code for the following is 691.

XVIII. Multiple Myeloma	9731-9733	18(181)
XIX. Leukemias	9803-9951	19
leukemia, NOS	9803,9805,9807-09	191
acute lymphocytic leukemia	9825	192
chronic lymphocytic leukemia	9827	193
other lymphocytic leukemia	9823,9828,9829	194
acute granulocytic leukemia	9865	195
chronic granulocytic leukemia	9867	196
other granulocytic leukemia	9863,9868,9869	197
monocytic leukemia	9893-9899	198

FIGURE 5

AVERAGE ANNUAL AGE-SPECIFIC CANCER INCIDENCE RATES:
ST. LOUIS PARK, RICHFIELD, EDINA, MPLS.-ST.PAUL
SMSA, WHITE FEMALES ONLY, BREAST, 1969-1971



SOURCE: 1

NUMBER OF CASES, INCIDENCE RATES, AND MANTEL-HAENSZEL SUMMARY CHI-SQUARE VALUES FOR CANCERS OF THE BREAST, WHITE FEMALES ONLY, 1969-1971

THREE YEAR TOTAL NUMBER OF CASES

Age Group	St. Louis Park	Edina	Richfield	MSP SMSA*
<15	0	0	0	0
15-24	0	0	0	1
25-34	1	2	0	53
35-44	10	13	6	215
45-54	23	22	19	448
55-64	33	12	8	499
65-74	14	9	2	447
75-84	12	6	5	369
85+	2	1	1	98
TOTAL	95	65	41	2130

AVERAGE ANNUAL AGE-SPECIFIC INCIDENCE RATES/100,000

<15	0	0	0	0
15-24	0	0	0	.19
25-34	9.17	28.67	0	14.36
35-44	122.19	132.68	74.38	74.49
45-54	235.10	221.82	195.59	162.23
55-64	441.77	184.50	149.81	230.51
65-74	298.76	238.10	71.45	272.29
75-84	520.16	321.03	333.33	382.05
85+	411.52	231.48	271.00	392.25
TOTAL	124.55	96.33	56.36	77.66

AVERAGE ANNUAL AGE-ADJUSTED INCIDENCE RATES/100,000**

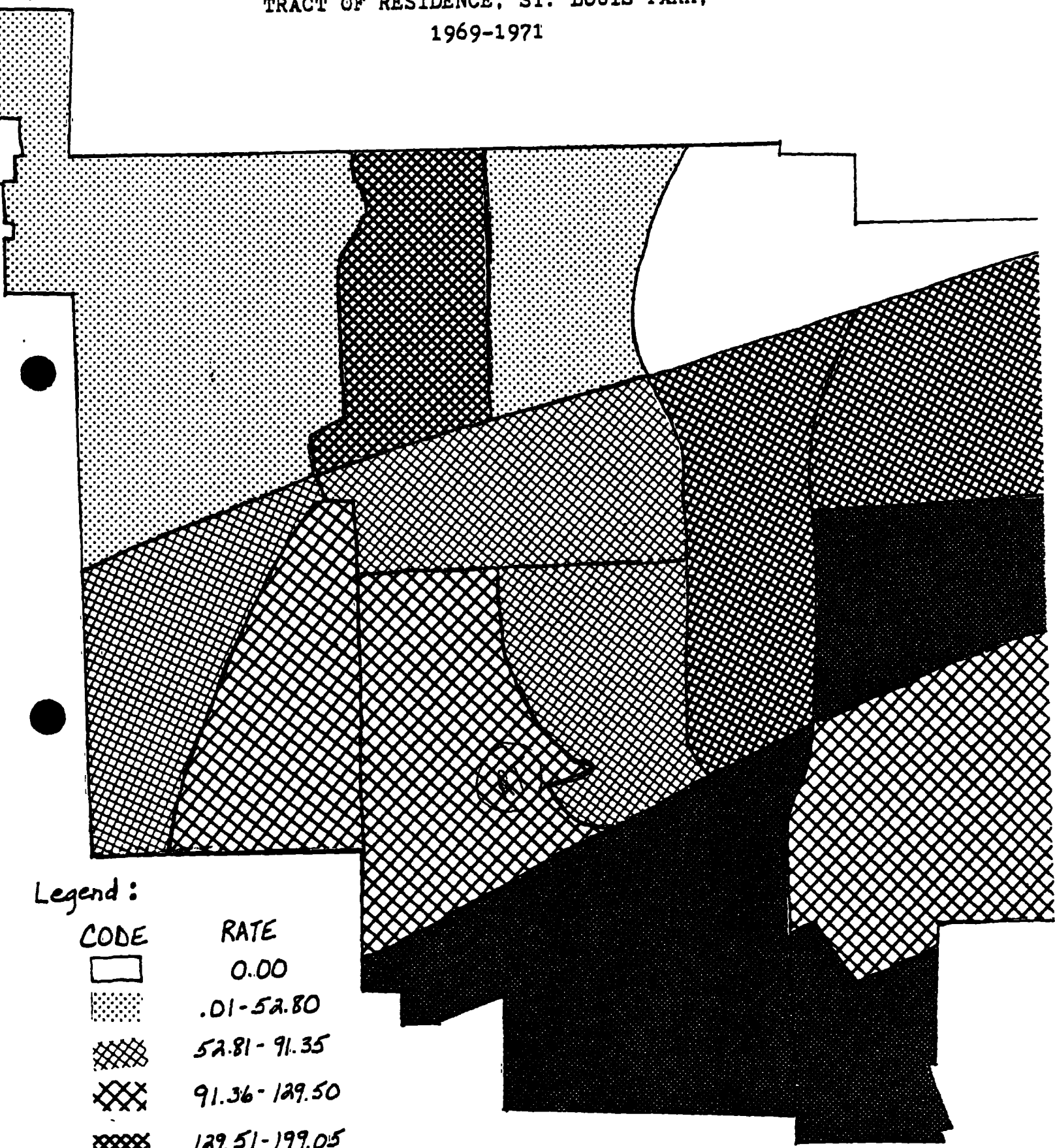
	112.58	82.39	57.83	77.66

Comparisons	Chi-Square Values	P Values
St. Louis Park vs Edina	3.38	$.10>\rho>.05$
St. Louis Park vs Richfield	10.85	$.001>\rho>.0005$
St. Louis Park vs MSP SMSA	13.64	$<.0005$

* Minneapolis-St. Paul Standard Metropolitan Statistical Area

** Adjusted to the SMSA population of white females, 1970.

AVERAGE ANNUAL INCIDENCE OF FEMALE BREAST CANCER
per 100,000 WHITE FEMALES by CENSUS
TRACT OF RESIDENCE, ST. LOUIS PARK,
1969-1971



[redacted]

NON-RESPONSIVE

[redacted]

shutdown. Nov. 1978

NON-RESPONSIVE